Analysis of Racial Differences in Incidence, Survival, and Mortality for Malignant Tumors of the Uterine Corpus

Mark E. Sherman, M.D.
Susan S. Devesa, Ph.D.

Department of Health and Human Services, National Institutes of Health, National Cancer Institute, Bethesda, Maryland.

BACKGROUND. In the United States, incidence rates for malignant tumors of the uterine corpus are lower among blacks than among whites, whereas mortality rates are higher among blacks. Reasons for the higher level of mortality among blacks have been debated.

METHODS. Using data from the Surveillance, Epidemiology, and End Results program, the authors compared incidence rates by histopathologic type for malignant tumors of the uterine corpus (including uterus, not otherwise specified) during the period 1992–1998 among white Hispanic, black, and white non-Hispanic patients. The authors also compared cumulative relative survival rates for blacks and whites by histopathologic type and by other factors, and they calculated estimated type-specific mortality rates.

RESULTS. Overall incidence (per 100,000 woman-years) of corpus malignancy was significantly lower among white Hispanics (14.04; 95% confidence interval [CI], 13.39–14.72) and blacks (15.31; 95% CI, 14.61–16.04) compared with white non-Hispanics (23.43; 95% CI, 23.06–23.81). Compared with white non-Hispanics, blacks had significantly higher incidence rates of serous/clear cell carcinoma (rate ratio, 1.85; 95% CI, 1.61–2.12), carcinosarcoma (rate ratio, 2.33; 95% CI, 1.99–2.72), and sarcoma (rate ratio, 1.56; 95% CI, 1.31–1.86). Survival was worse for blacks than for whites in every histopathologic category and in 'usual' types of endometrial adenocarcinoma, stratified by stage, grade, and age. Rare aggressive tumor types accounted for 53% of mortality among blacks, compared with 36% among whites.

CONCLUSIONS. Less favorable outcomes for usual types of endometrial adenocarcinoma and for rare aggressive tumors contribute equally to the relatively high mortality due to corpus cancer among black women. ***Cancer* 2003;98:176–86.**
*Published 2003 by the American Cancer Society.**

KEYWORDS: uterus, malignant, neoplasm, incidence, survival, mortality, SEER.

In the United States, the incidence of malignant tumors of the uterine corpus is considerably lower among blacks compared with whites; however, blacks have less favorable survival and mortality rates.[1,2] A recent metaanalysis that compared the survival of blacks and whites who had received comparable treatment for similarly staged malignancies found that blacks had twice the mortality rate of whites for corpus cancer.[3] The reasons for these differences are not well understood.

The great majority of malignant corpus tumors are endometrial adenocarcinomas, of which endometrioid adenocarcinomas represent the predominant histopathologic type. Most endometrioid adenocarcinomas seem to develop slowly from endometrial hyperplasia in the setting of hormonal imbalance and are associated with an

The authors thank Mr. John Lahey for expert computer programming support and Drs. Pamela Mink and James V. Lacey, Jr., for critical review of this article.

Address for reprints: Mark E. Sherman, M.D., The National Cancer Institute, Division of Cancer Epidemiology and Genetics, 6120 Executive Blvd., Room 7080, Rockville, MD 20892-7374; Fax: (301) 402-0916; E-mail: shermanm@mail.nih.gov

The views expressed herein do not necessarily reflect the views of the National Cancer Institute or the U.S. Government.

Published 2003 by the American Cancer Society*

DOI 10.1002/cncr.11484

excellent prognosis when detected and adequately treated at an early stage.[1,2,4] The higher incidence of endometrioid adenocarcinoma among whites compared with blacks accounts for the higher overall incidence of endometrial carcinoma among whites. Data demonstrating that blacks tend to present with more advanced–stage disease[5–14] and receive less aggressive treatment[8] than do whites suggest that providing blacks with improved health care could reduce their endometrial cancer mortality. Nonetheless, worse survival for blacks with readily curable forms of endometrial carcinoma may not account entirely for the racial disparity in mortality.

Several studies have suggested that aggressive uterine malignancies, including serous and clear cell endometrial adenocarcinomas, carcinosarcoma, and sarcoma, account for a disproportionate percentage of tumors among black women.[7–12,15,16] Studies also suggest that the etiology and pathogenesis of some aggressive types of endometrial carcinoma differ from those of the most common type of endometrial carcinoma, endometrioid adenocarcinoma.[4,17] Specifically, pure serous carcinoma appears to develop from atrophic, rather than hyperplastic, epithelium and may not be associated with typical risk factors for endometrial malignancy.[4,18] Consequently, part of the higher mortality among blacks may reflect differences in etiologic exposure, genetics, or other factors that lead to higher rates of aggressive tumors.

Although differences between blacks and whites in the occurrence and behavior of malignant uterine tumors have been studied,[5–7,9–14,19–21] the reason for higher mortality among blacks continues to be understood incompletely. As a result, we performed a detailed analysis of population-based incidence, survival, and mortality rates for the period 1992–1998 to determine the relative contributions of different factors to mortality rates for blacks and whites. Specifically, we compared the incidence, by histopathologic type, of malignant tumors of the uterine corpus and uterus, not otherwise specified (NOS), among white Hispanics and blacks with the incidence among white non-Hispanics, using data from the Surveillance, Epidemiology, and End Results (SEER) program. We also performed a detailed analysis of survival and mortality data to assess the relative contributions of different factors to racial disparities in outcome.

MATERIALS AND METHODS

Ascertainment of Cases and Deaths

Since 1992, the SEER program, administered by the National Cancer Institute, has collected population-based data on cancer incidence through 11 registries, which represent approximately 14% of the United States population.[22] The incidence and survival analyses in the current study were based on data collected by seven of those registries—San Francisco–Oakland, Connecticut, metropolitan Detroit, New Mexico, metropolitan Atlanta, San Jose–Monterey, and Los Angeles–for white Hispanics, blacks, and white non-Hispanics. The four registries serving the fewest Hispanics and blacks were excluded from these tabulations. To estimate the percentage of deaths caused by a specific histopathologic type, we frequency-matched mortality data for the years 1992–1998 to incidence data for the years 1973–1998 using data collected by 9 SEER registries (representing almost 10% of the U.S. population)—San Francisco–Oakland, Connecticut, metropolitan Detroit, Hawaii, Iowa, New Mexico, Seattle (Puget Sound), Utah, and metropolitan Atlanta. These registries are the oldest ones in SEER and therefore included the most complete records (i.e., those that covered the most years) of incidence data for fatal cases.

Histopathologic Classification of Cases

Analyses of incidence survival were limited to invasive tumors with site codes of uterine corpus or uterus, NOS (excluding choriocarcinoma), diagnosed between 1992 and 1998. Specific histopathologic tumor types, coded in the SEER database using the *International Classification of Diseases for Oncology (2nd Edition)*,[23] were grouped into five categories according to clinical behavior (Table 1). Category I included common indolent types of endometrial adenocarcinoma, which were coded as endometrioid,
mucinous, or adenocarcinoma, NOS. Inclusion of adenocarcinoma, NOS, in Category I is justified, because endometrioid adenocarcinoma is the most common type of endometrial adenocarcinoma (the 'usual' type), and therefore, diagnoses of adenocarcinoma, NOS, most likely corresponded to cases of endometrioid adenocarcinoma. Category II encompassed serous and clear cell adenocarcinomas, two uncommon, highly aggressive types of endometrial adenocarcinoma. Areas of serous and clear cell differentiation often are found together in carcinomas that show mixed histopathologic patterns.[4,18] Category III was limited to carcinosarcoma (malignant mixed mullerian tumor), a unique tumor type that is composed of both malignant glands and stroma and has a different age-specific incidence pattern than do other malignant uterine tumors containing malignant stroma.[21] Category IV included tumors such as leiomyosarcoma, endometrial stromal sarcoma, and adenosarcoma (a tumor composed of glands that appear to be benign and malignant stroma), in which only the stroma is malignant. Tumors that did not fit in categories I–IV were placed in Category V.

TABLE 1
Histopathologic Categories of Malignant Uterine Corpus Tumors, Based on ICD-O-2 Codes

Histopathologic category	Main histopathologic type(s)	ICD-O-2 codes
I	Adenocarcinoma, NOS; endometrioid adenocarcinoma; mucinous adenocarcinoma	8050, 8140–8141, 8143, 8210, 8211, 8260–8263, 8323, 8340, 8380, 8381, 8440, 8470, 8471, 8480, 8481, 8490, 8550, 8560, 8570–8573
II	Serous adenocarcinoma; clear cell adenocarcinoma	8310, 8441, 8460–8462
III	Carcinosarcoma	8950, 8951, 8980, 8981
IV	Leiomyosarcoma; endometrial stromal sarcoma; adenosarcoma	8890, 8891, 8896, 8910, 8930, 8933
V	Other tumor types	8000–8004, 8010, 8012, 8020–8022, 8031, 8032, 8041, 8052, 8070–8073, 8075, 8076, 8120, 8130, 8200, 8230, 8244, 8246, 8510, 8650, 8680, 8800–8802

ICD-O-2: International Classification of Diseases (2nd Edition); NOS: not otherwise specified.

Analysis

Using SEER*STAT software (National Cancer Institute, Bethesda, MD),[24] incidence data for white Hispanics and white non-Hispanics were extracted from the file "SEER 11 sub for Hispanics race recode Z" after exclusion of the four registries mentioned earlier. Data for black women were extracted from the file "SEER 11 sub for expanded races recode Y."

Incidence rates per 100,000 woman-years, age-adjusted to the 1970 U.S. standard, were tabulated. Data regarding the five histopathologic categories defined earlier were tabulated by race and ethnicity. Tumors in Category I subsequently were stratified by stage (localized, regional, distant, or unstaged),[22] grade (well-differentiated, moderately differentiated,[23] poorly differentiated, undifferentiated, or unknown), and patient age (25–44, 45–54, 55–74, or $\geq$ 75 years). Rates for white Hispanics and blacks were compared with those for white non-Hispanics. Defining c as the number of cases, p as the number of women, and the incidence rate r as c/p, the 95% confidence intervals (CIs) for incidence rates were calculated using the formula $CI = r \pm 1.96 \times r/\sqrt{c}$; the 95% CIs for rate ratios were computed using the formula

$$CI = \exp[\ln(r1/r2)] \pm 1.96 \times \sqrt{(1/c1 + 1/c2)}.$$

We compared the clinical outcomes of black and white patients with malignant uterine tumors by calculating the cumulative relative survival, which controls for competing causes of death. (Specific data for Hispanics were not available.) Cumulative relative survival was computed by comparing the survival rates of black and white patients with malignant tumors of the uterine corpus or uterus, NOS, with the estimated survival rate of the total population of women, matched for age and race. Cumulative relative survival, expressed as a percentage, was plotted at yearly intervals for 5 years following diagnosis for black and white women stratified by histopathologic category (I–IV). To gain a better understanding of the outcomes associated with the large, heterogeneous group of tumors included in Category I, we performed additional survival analyses that stratified patients according to three key prognostic factors—stage, grade, and age—and plotted the resulting data in similar fashion. We did not perform further survival analyses for tumors in Categories II–IV, which are known to be associated with a relatively poor prognosis. Tumors in Categories II and III generally are considered to be high-grade by definition.

Mortality data based on death certificates are not available by histopathologic type. As a result, we estimated the relative contribution of tumors in a given histopathologic category (I–V) to total corpus cancer mortality for blacks and whites during the period 1992–1998 using an approach similar to the one described by Chu et al.[25] According to data from the National Center for Health Statistics (NCHS), there were 443 uterine corpus cancer deaths among blacks and 3160 deaths among whites in the 9 SEER areas during this period, yielding mortality rates of 5.0 and 3.1 per 10^5 woman-years for blacks and whites, respectively. We used the long-term 1973–1998 SEER files (from the nine registries specified earlier) to identify women diagnosed with corpus or uterine cancer, NOS, who eventually died of their tumors during the period 1992–1998. We used the incidence data for 1973–1998 to determine the histopathologic categories of fatal cases by race and the percentage of fatal cases represented by each category. These percentages then were multiplied by the

TABLE 2
Incidence of Malignant Uterine Corpus Tumors by Histopathologic Category, Race, and Ethnicity (1992–1998)

		White Hispanic		Black			White non-Hispanic		
Histopathologic category	No. of cases	Incidence[a] (95% CI)	Rate ratio[b] (95% CI)	No. of cases	Incidence[a] (95% CI)	Rate ratio[b] (95% CI)	No. of cases	Incidence[a] (95% CI)	Rate ratio[b]
All categories	1836	14.04 (13.39–14.72)	0.60 (0.57–0.63)	1844	15.31 (14.61–16.04)	0.65 (0.62–0.69)	16,512	23.43 (23.06–23.81)	Ref.
I[c]	1484	11.39 (10.80–12.00)	0.57 (0.54–0.60)	1100	9.20 (8.66–9.77)	0.46 (0.43–0.49)	13,989	20.14 (19.79–20.49)	Ref.
II[d]	102	0.85 (0.69–1.03)	0.72 (0.59–0.89)	251	2.16 (1.90–2.45)	1.85 (1.61–2.12)	908	1.17 (1.09–1.26)	Ref.
III[e]	74	0.63 (0.49–0.79)	0.80 (0.63–1.02)	210	1.82 (1.58–2.08)	2.33 (1.99–2.72)	613	0.78 (0.72–0.85)	Ref.
IV[f]	122	0.80 (0.66–0.96)	1.01 (0.83–1.23)	166	1.24 (1.05–1.45)	1.56 (1.31–1.86)	518	0.79 (0.72–0.87)	Ref.
V[g]	54	0.38 (0.29–0.51)	0.70 (0.52–0.92)	117	0.90 (0.74–1.09)	1.63 (1.33–1.99)	484	0.55 (0.50–0.61)	Ref.

CI: confidence interval; Ref.: referent group.
[a] Rate per 10^5 woman-years, age-adjusted using the 1970 U.S. standard population.
[b] Relative to white non-Hispanics.
[c] Usual types of endometrial adenocarcinoma, including endometrioid adenocarcinoma.
[d] Serous/clear cell carcinoma.
[e] Carcinosarcoma.
[f] Pure sarcoma.
[g] Tumor types not included in Categories I–IV.

total NCHS corpus cancer mortality rates for blacks and whites during the period 1992–1998 to estimate mortality rates for specific histopathologic categories by race. Possible reasons for missing incidence data regarding fatal cases include diagnosis before 1973, diagnosis outside the catchment areas of the nine SEER registries, and lack of diagnostic confirmation.

RESULTS

Incidence Rates by Race and Ethnicity (1992–1998)

The overall incidence of tumors classified as corpus and uterus, NOS, was significantly lower for white Hispanics (14.04; 95% CI, 13.39–14.72) and blacks (15.31; 95% CI, 14.61–16.04) compared with white non-Hispanics (23.43; 95% CI, 23.06–23.81) (Table 2). Rates for Category I tumors were significantly higher for white non-Hispanics compared with the other racial/ethnic groups; this difference accounted for the large difference in overall incidence of malignant tumors. Compared with white non-Hispanics, white Hispanics had lower rates of Category II and Category III tumors, although the rate ratio for Category III neoplasms fell slightly short of statistical significance. Blacks had significantly higher incidence rates than did white non-Hispanics for clinically aggressive tumors in Categories II–V. Rate ratios comparing blacks with white non-Hispanics were 1.85 for Category II, 2.33 for Category III, 1.56 for Category IV, and 1.63 for Category V.

Incidence of Usual Types of Endometrial Adenocarcinoma (Category I), 1992–1998, Stratified by Race and Ethnicity, Followed by Stage, Grade, and Age

Stage-specific rates of histopathologic Category I tumors were uniformly lower among white Hispanics compared with white non-Hispanics (Table 3). Rates for localized and regional disease were significantly lower for blacks compared with white non-Hispanics, whereas rates for distant and unstaged disease were more similar in these two groups.

The incidence rates of well-differentiated, moderately differentiated, and poorly differentiated Category I tumors all were significantly lower among white Hispanics compared with white non-Hispanics. The rate ratio approached 1.0 for undifferentiated carcinomas; however, this ratio was calculated based on a small number of cases (Table 3). In contrast, blacks had significantly lower incidence rates than did white non-Hispanics for well-differentiated and moderately differentiated tumors, but they had more similar rates for poorly differentiated and undifferentiated tumors. Tumors of unknown grade were significantly less common among white Hispanics and blacks compared with white non-Hispanics.

Irrespective of race and ethnicity, incidence rates of Category I tumors increased sharply until age 55 years (Table 3). Rates for white Hispanics and white non-Hispanics were similar for women ages 25–44 years, whereas rates for white Hispanics age $\geq$ 45 years and for black women of all ages were significantly lower than the rates for white non-Hispanics. Age-specific incidence rates for women ages 55–74

TABLE 3
Incidence of Usual Types of Endometrial Adenocarcinoma (Category I) by Stage, Grade, and Age for White Hispanic, Black, and White Non-Hispanic Women (1992–1998)

	White Hispanic			Black			White non-Hispanic		
Characteristic	No. of cases	Incidence[a] (95% CI)	Rate ratio[b] (95% CI)	No. of cases	Incidence[a] (95% CI)	Rate ratio[b] (95% CI)	No. of cases	Incidence[a] (95% CI)	Rate ratio[b]
Stage									
Localized	1094	8.41 (7.90–8.94)	0.53 (0.50–0.56)	691	5.78 (5.35–6.24)	0.36 (0.34–0.39)	10,859	15.87 (15.56–16.18)	Ref.
Regional	244	1.88 (1.65–2.14)	0.72 (0.63–0.82)	194	1.63 (1.40–1.88)	0.62 (0.54–0.72)	1903	2.62 (2.50–2.75)	Ref.
Distant	89	0.70 (0.56–0.87)	0.71 (0.57–0.89)	116	0.98 (0.81–1.18)	1.00 (0.82–1.21)	713	0.99 (0.91–1.07)	Ref.
Unstaged	57	0.40 (0.30–0.52)	0.59 (0.45–0.78)	99	0.81 (0.65–0.99)	1.21 (0.97–1.50)	514	0.67 (0.61–0.74)	Ref.
Grade (differentiation)									
Well	654	4.86 (4.48–5.26)	0.51 (0.47–0.55)	345	2.85 (2.55–3.18)	0.30 (0.27–0.33)	6434	9.53 (9.29–9.78)	Ref.
Moderate	509	3.99 (3.65–4.37)	0.59 (0.54–0.65)	362	3.06 (2.75–3.39)	0.45 (0.41–0.50)	4723	6.76 (6.56–6.97)	Ref.
Poor	240	1.91 (1.67–2.17)	0.75 (0.66–0.86)	273	2.30 (2.03–2.60)	0.91 (0.80–1.03)	1908	2.54 (2.43–2.67)	Ref.
Undifferentiated	26	0.21 (0.14–0.31)	0.92 (0.61–1.39)	33	0.28 (0.19–0.39)	1.21 (0.83–1.76)	167	0.23 (0.19–0.27)	Ref.
Unknown	55	0.41 (0.31–0.54)	0.38 (0.29–0.50)	87	0.71 (0.57–0.89)	0.66 (0.53–0.83)	757	1.08 (1.00–1.16)	Ref.
Age (yrs)									
25–44	231	3.89 (3.40–4.43)	0.95 (0.82–1.11)	91	1.92 (1.55–2.37)	0.47 (0.38–0.59)	730	4.07 (3.78–4.38)	Ref.
45–54	323	20.60 (18.40–22.99)	0.63 (0.56–0.71)	162	11.71 (9.97–13.68)	0.36 (0.31–0.42)	2183	32.46 (31.11–33.85)	Ref.
55–74	747	43.85 (40.76–47.12)	0.54 (0.50–0.58)	640	38.81 (35.85–41.95)	0.48 (0.44–0.52)	7626	81.25 (79.39–83.13)	Ref.
75+	175	36.75 (31.46–42.71)	0.45 (0.39–0.52)	206	39.35 (34.12–45.18)	0.48 (0.42–0.56)	3449	81.57 (78.82–84.39)	Ref.

CI: confidence interval; Ref.: referent group.

[a] Rate per 10^5 woman-years, age-adjusted using the 1970 U.S. standard population.

[b] Relative to white non-Hispanics.

years and women age ≥ 75 years were similar within every racial/ethnic group.

Cumulative Relative Survival Rates by Race and Histopathologic Category

Cumulative relative survival was considerably better for women with Category I neoplasms compared with those with Category II–IV neoplasms; survival also was better, regardless of racial/ethnic group, for women with Category IV neoplasms than for those with Category II or III neoplasms (Fig. 1). Survival was worse for blacks compared with whites (white Hispanics plus non-white Hispanics) for all histopathologic categories and years of follow-up. The survival curves, stratified by race, for women with Category I tumors were strikingly different from each other; survival for blacks declined linearly to 69.1% over 5 years, whereas the curve for whites was nearly flat, with 89.8% survival after 5 years. The 5-year survival rates for blacks with Category II and Category III tumors were 35.8% and 32.8%, respectively, compared with 49.9% and 43.3%, respectively, for whites, and generally were parallel. The survival rates among blacks and whites were more similar in Category IV, respectively 54.9% and 57.0%.

Cumulative Relative Survival Rates for Usual Types of Endometrial Adenocarcinoma (Category I) by Race and Stage

Stage at diagnosis had a greater impact on survival than did age or tumor grade for women diagnosed with Category I tumors (Figs. 2–4). Survival was worse for blacks than for whites for all stages and periods of follow-up (Fig. 2). For localized disease, the survival rate for blacks decreased slightly for 2 years and then decreased somewhat more rapidly, to 89.7% after 5 years. The survival rate for whites was 97.9% after 5 years. The survival disparity for women with regional disease was greater than any other disparity observed in stage-specific racial comparisons. Survival for blacks with regional disease decreased sharply over time, to 38.3% at 5 years. In contrast, the rate of decrease in survival rate among whites with regional disease slowed after 2 years; cumulative relative survival was 72.7% after 5 years. The survival rate at 5 years from diagnosis was 13.1% for blacks with distant disease, compared with 29.4% for whites with distant disease.

Cumulative Relative Survival Rates for Usual Types of Endometrial Adenocarcinoma (Category I) by Race and Grade

The survival rate for blacks with well-differentiated Category I tumors was 91.0% at 5 years, compared with 98.8% for whites (Fig. 3). The survival curve for

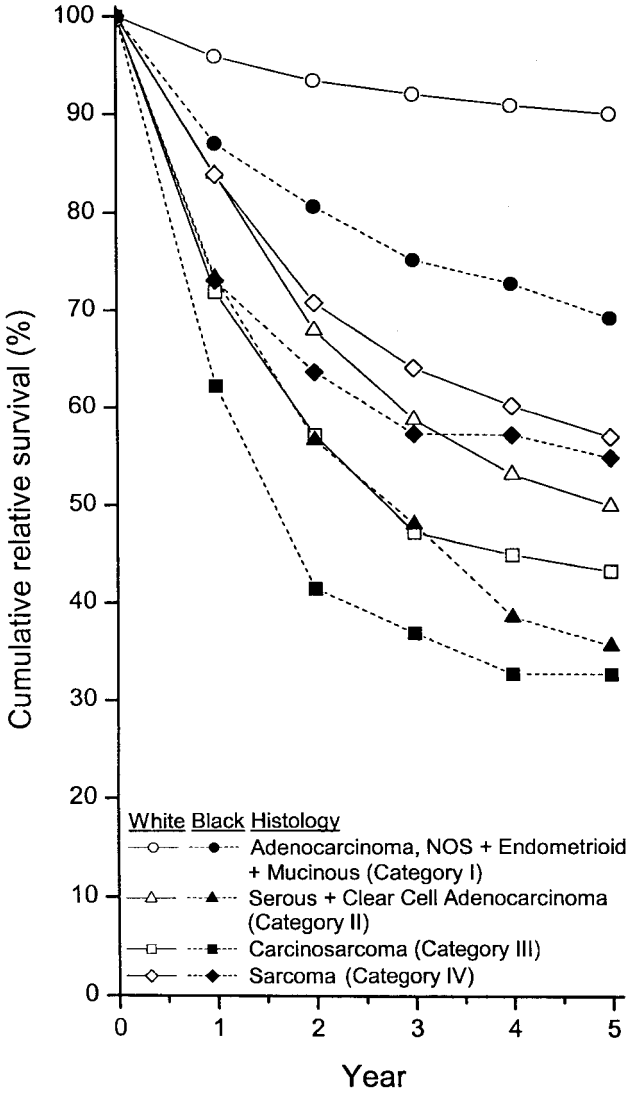

FIGURE 1. Cumulative relative survival curves for women diagnosed with corpus cancer or uterine cancer, not otherwise specified (NOS), by race and histopathologic category (1992–1998).

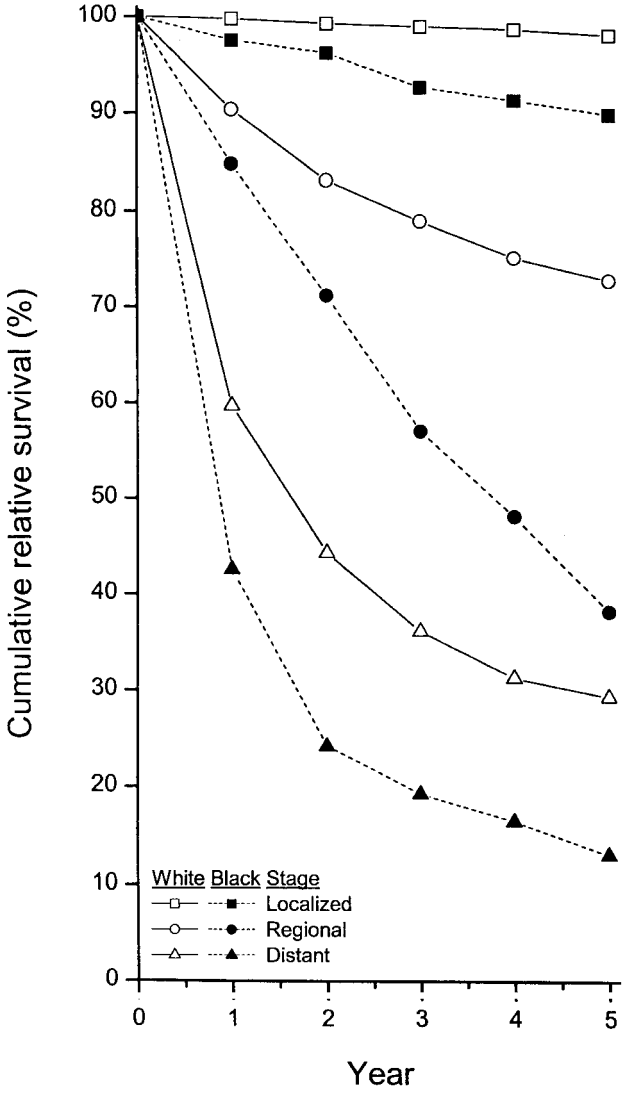

FIGURE 2. Cumulative relative survival curves for women diagnosed with usual types of endometrial adenocarcinoma (Category I), by race and disease stage (1992–1998).

blacks with well-differentiated tumors was nearly identical to the curve for whites with moderately differentiated tumors. Survival for blacks with poorly differentiated or undifferentiated tumors was 38.7% at 5 years, compared with 62.5% for whites.

Cumulative Relative Survival Rates for Usual Types of Endometrial Adenocarcinoma (Category I) by Race and Age

Survival rates among blacks declined steadily with increasing age (Fig. 4). In contrast, white women ages 25–44 years and white women ages 45–54 years experienced nearly identical excellent survival; worse survival was observed for whites in the 2 oldest age groups. Differences in survival between older blacks and older whites were striking. The 5-year survival rate for blacks ages 55–74 years was 66.5%, compared with 89.8% for whites. Similarly, the 5-year survival rate for blacks $\geq$ 75 years of age was 52.0%, compared with 83.7% for whites.

Mortality among Black and White Women by Histopathologic Category, 1992–1998

Incidence data reported to SEER for cases diagnosed during the period 1973–1998 included 353 (79.7%) of 443 blacks and 2813 (89.0%) of 3160 whites who died of uterine corpus cancer (according to NCHS records) between 1992 and 1998. Estimated mortality rates

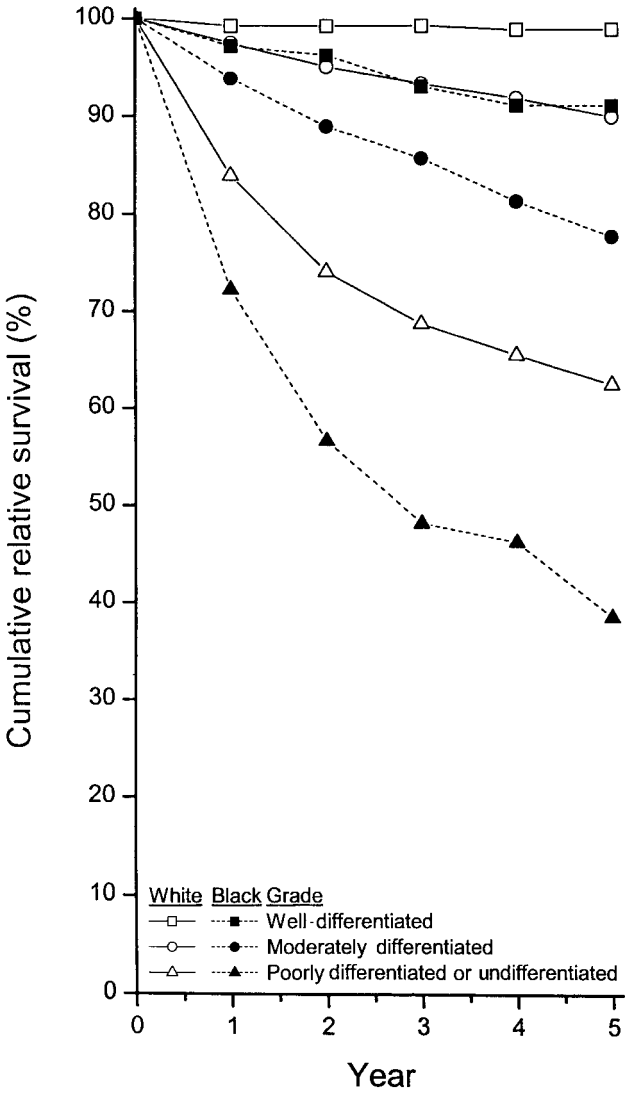

FIGURE 3. Cumulative relative survival curves for women diagnosed with usual types of endometrial adenocarcinoma (Category I), by race and tumor grade (1992–1998).

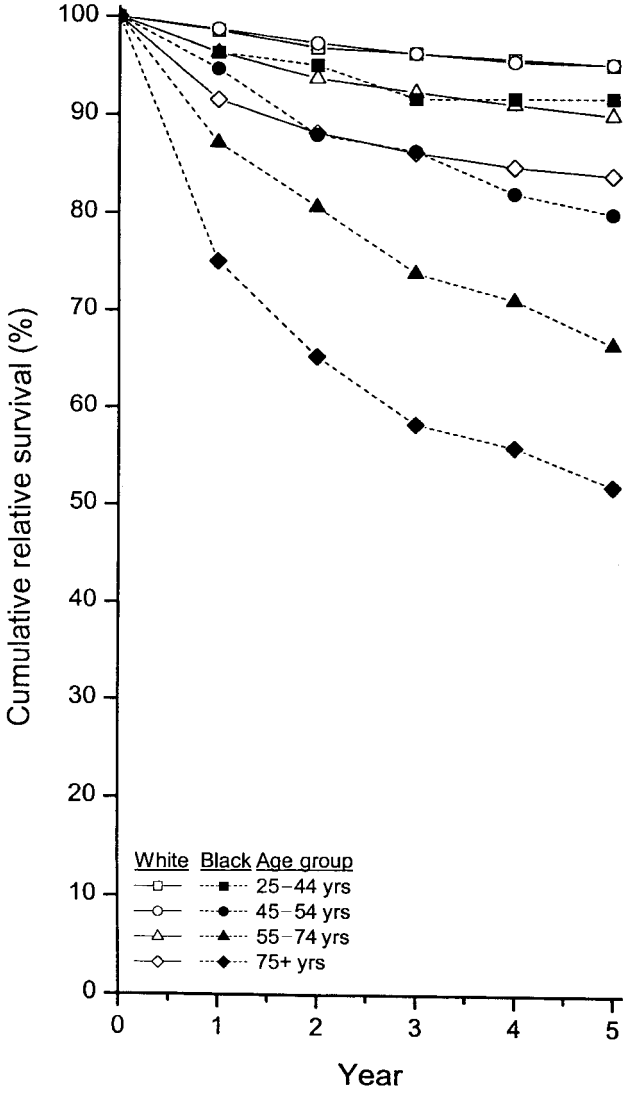

FIGURE 4. Cumulative relative survival curves for women diagnosed with usual types of endometrial adenocarcinoma (Category I), by race and age (1992–1998).

were higher for blacks than for whites for all histopathologic categories (Table 4). The estimated mortality rate for blacks with Category I tumors was 2.35, compared with 1.98 for whites. Absolute racial differences in mortality rates were even greater for Categories II and III than for Category I. Approximately 53% of the total mortality among blacks was associated with Category II–V tumors, whereas only 36% of the mortality among whites was related to these types of tumors.

DISCUSSION

Our analysis of SEER data for the period 1992–1998 demonstrated that white Hispanics and blacks had similar incidence rates of malignant uterine corpus tumors, whereas the rate for white non-Hispanics was significantly higher. This difference was attributable largely to the lower incidence of typical indolent types of endometrial adenocarcinoma among white Hispanics and blacks.

White Hispanics had lower incidence rates than did white non-Hispanics for most individual histopathologic tumor types; white Hispanics also had a lower overall incidence of uterine tumors. Blacks had significantly higher rates than did white non-Hispanics for aggressive tumor types, including serous and clear cell carcinomas (rate ratio, 1.85), carcinosarcoma (rate ratio, 2.33), and sarcoma (rate ratio, 1.56). Previous studies have demon-

TABLE 4
Partitioned Mortality Rates by Race (1992–1998)[a]

Histopathologic category	Blacks		Whites	
	No. of cases (%)	Mortality[b]	No. of cases (%)	Mortality[b]
I[c]	166 (47.03)	2.35	1794 (63.78)	1.98
II[d]	62 (17.56)	0.88	342 (12.16)	0.38
III[e]	58 (16.43)	0.82	271 (9.63)	0.30
IV[f]	35 (9.92)	0.50	161 (5.72)	0.18
V[g]	32 (9.07)	0.45	245 (8.71)	0.27
Total[h]	353 (100.0)	5.0	2813 (100.0)	3.1

[a] Total and category-specific numbers based on SEER cases that were diagnosed between 1973 and 1998 and were associated with death due to corpus cancer between 1992 and 1998.

[b] Category-specific mortality rates were estimated by applying category-specific percentages to the total National Center for Health Statistics rate. Mortality rate per 10^5 woman-years, age-adjusted using the 1970 U.S. standard population.

[c] Usual types of endometrial adenocarcinoma, including endometrioid adenocarcinoma.

[d] Serous/clear cell carcinoma.

[e] Carcinosarcoma.

[f] Pure sarcoma.

[g] Tumor types not included in Categories I–IV.

[h] Total mortality rate based on National Center for Health Statistics data.

strated that aggressive tumor types account for a higher percentage of total malignancies among blacks compared with whites.[7,8,10–12,16] Nonetheless, demonstrating that population-based incidence rates of aggressive tumors are higher among blacks than among whites is important, because it establishes that the higher percentage of aggressive tumors among blacks truly reflects increased occurrence, rather than a relative increase related to lower rates for the usual types of endometrial carcinoma.

An analysis of data from the California Cancer Registry (1988–1992) on 14,487 women (including 449 blacks and 11,992 white non-Hispanics) showed that whites and blacks had similar rates of high-grade adenocarcinomas, but 88% of the cases included in this category were Grade 3 or 4 adenocarcinomas; serous and clear cell carcinomas accounted for only 12% of the cases in this group and were not analyzed separately.[16] Another analysis, which used data from the Michigan state registry (1985–1994), found that the rate of aggressive adenocarcinoma (serous, clear cell, or undifferentiated carcinoma) for blacks was 1.84 per 100,000 woman years, compared with 1.29 for whites, but the authors concluded that these results were similar.[11] Our analysis of recent SEER data on more than 20,000 corpus tumors demonstrates that there are racial differences in the incidence rates of specific histopathologic types of endometrial cancer. In addition, the data from the current study indicate that previously identified racial disparities in tumor types have persisted through the 1990s, despite shifts in diagnostic criteria.[26] The current analysis also demonstrates that the previously reported higher incidence of sarcoma among blacks compared with whites persists.[21]

The Behavioral Risk Factor Surveillance System found a 2.4% higher frequency of self-reported hysterectomy among black non-Hispanics compared with white non-Hispanics.[27] Similarly, the National Health Interview Survey found that a history of hysterectomy was 1.4% more common among blacks.[27] Incidence rates in SEER are not adjusted for the prevalence of hysterectomy and therefore underestimate uterine cancer incidence among women at risk.[28] Overall rates of hysterectomy are similar for blacks and whites; however, rates among premenopausal blacks are higher than among whites, whereas rates among postmenopausal whites are higher than among blacks.[29] Furthermore, the indications for hysterectomy differ considerably between blacks and whites; blacks undergo operations more frequently than do whites for leiomyomata, but they undergo operations less often for most other common indications.[30] If endometrial cancer risk factors differ among women undergoing hysterectomy for different indications, then hysterectomy rates may differentially affect cancer risk among black and white women.

Racial differences in the prevalence of risk factors may account for disparities in incidence. Use of unopposed estrogen and obesity are two risk factors strongly associated with endometrial cancer,[1] but neither factor appears to account for the racial disparities in tumor incidence. Historically, blacks have used unopposed estrogen more frequently than have whites, although whites have used combined therapy more frequently.[31] Furthermore, the increase in endometrial cancer rates that was attributable to the administration of unopposed estrogen to women with intact uteri was reversed 2 decades ago when this practice was halted.[1] Paradoxically, obesity[32] and physical inactivity[33] are more common among blacks than among whites; this finding might be expected to result in relatively higher endometrial cancer rates among blacks. Other risk factors, such as age at menarche and age at menopause, are similar for blacks and whites.[34,35]

Parity, smoking, and oral contraceptive use are protective for usual types of endometrial adenocarcinoma.[1,36,37] In 2000, fertility rates, expressed as the number of births per 1000 women ages 15–44 years, were 105.9 for Hispanics, 71.4 for blacks, and 58.7 for white non-Hispanics.[38] Among blacks, fertility rates decreased by 19% between 1990 and 1996 and then stabilized, suggesting that older blacks may have had even more protection due to parity than did younger

blacks. Reported frequencies of current smoking among black and white non-Hispanics are similar, although the frequency of former smokers is lower among blacks.[33] Current and former smoking are less common among Hispanics compared with either white or black non-Hispanics. Oral contraceptive use is somewhat more frequent among white Hispanics and black non-Hispanics compared with white non-Hispanics.[39] Of these factors, the much higher parity among white Hispanics and blacks compared with white non-Hispanics seems most likely to account for a considerable portion of the observed differences in incidence rates.

Elevated serum levels of estrogens have been associated with increased risk among postmenopausal women (but not among premenopausal women).[40,41] Manson et al.[42] found that circulating levels of dehydroepiandrosterone sulfate (DHEAS), an estradiol precursor, consistently were lower among blacks ages 35–47 years compared with whites; they also reported that levels of estradiol were lower among blacks on the first of 4 serial monthly measurements. Levels of DHEAS and estradiol decreased sharply with increasing age among blacks, whereas among whites, DHEAS levels decreased less rapidly and estradiol levels remained constant. Replication of these data in an epidemiologic study of endometrial adenocarcinoma may help clarify the reasons for racial differences in cancer incidence.

It has been hypothesized that aggressive types of endometrial adenocarcinoma may have a different etiology than do usual types of endometrial carcinoma.[4,17] Pure serous carcinoma typically arises directly from atrophic endometrium, rather than from endometrial hyperplasia. Sherman et al.[43] reported that serous carcinoma is less strongly related to high body mass index, exogenous estrogen use, and elevated serum levels of estrogenic hormones than is endometrioid carcinoma. A retrospective case-control study comparing living patients with serous carcinoma with healthy control patients found that body mass indices were similar at diagnosis, although cases reported a slightly higher nonobese weight at age 18 years (56.2 kg, compared with 53.5 kg for control patients) and more frequent use of unopposed estrogen.[44] Given that blacks have a much lower incidence of endometrioid adenocarcinoma than do whites, it may be the case that blacks are less exposed to estrogens and therefore more likely to develop tumors (e.g., serous carcinoma) that arise from atrophic endometrium. The extremely high fertility rate among Hispanics may be protective against several types of uterine tumors, although risk factor data for carcinosarcoma and sarcoma are limited.[45,46]

As was expected, white Hispanics had lower incidence rates than did white non-Hispanics for all stages and grades of usual types of endometrial adenocarcinoma. Blacks had lower rates than did white non-Hispanics only for Category I tumors staged as local or regional and Category I tumors graded as well-differentiated or moderately differentiated; rates for tumors staged as distant and for poorly differentiated tumors were similar. The observed shift toward higher stage and grade among blacks with usual types of endometrial adenocarcinoma is consistent with previous reports.[5–12,14–16,20] Possible explanations for these findings can be classified either as clinical factors related to health care access, diagnosis, and treatment, or as biologic factors that predispose blacks to develop more aggressive tumors. Conclusions regarding the relative contributions of clinical and biologic factors to the less favorable outcome experienced by blacks vary.[5–15] Although several studies have found that the symptomatic period before presentation or treatment is similar for blacks and whites,[10,12,20] additional studies evaluating possible racial disparities in health care access, diagnosis, and treatment are needed.

Age-specific incidence patterns for usual types of endometrial adenocarcinoma also differed by race and ethnicity. The incidence rates of these tumors among women ages 25–44 years were similar for white Hispanics and white non-Hispanics; however, among white Hispanics, the rates did not increase as rapidly with increasing age, resulting in a lower overall incidence of these tumors. In all age groups, incidence rates for blacks were considerably lower than for white non-Hispanics.

Overall survival among blacks with usual types of endometrial adenocarcinoma decreased dramatically over the entire follow-up period, whereas among whites, survival decreased during the first year and then decreased little over the next 4 years. Survival for blacks was worse than it was for whites for every stage, grade, and age group. The most striking racial differences in survival were associated with tumors staged as regional, tumors graded as poorly differentiated, and tumors occurring in women age $\geq$ 55 years. Data indicating that blacks receive less aggressive treatment than do whites[8] suggest that differences in health care may account at least partially for racial disparities in survival.

For serous and clear cell carcinomas, carcinosarcoma, and sarcoma, survival curves for blacks and whites paralleled each other but showed much worse survival for blacks at each follow-up time. The combination of higher incidence and lower survival among blacks with aggressive disease highlights the impact that these tumors have on mortality in this racial

group. Furthermore, our analysis of mortality rates partitioned by histopathologic type demonstrated that among blacks, unusual aggressive types of malignant tumors caused 53% of tumor-related deaths, compared with 36% of tumor-related deaths among whites.

Using SEER data, which are broadly representative of the U.S. population, we have presented an analysis of recent uterine cancer incidence, survival, and mortality. Limitations of our study include incomplete follow-up; classification of many tumors as adenocarcinoma, NOS; and the lack of expert histopathologic review. In addition, self-reporting of race and ethnicity may be subjective, and the possibility of intraracial heterogeneity was not explored. Finally, our analysis of type-specific mortality was limited to 79.7% of blacks and 89.0% of whites because of incomplete ascertainment of incidence data due to relocation and other factors. Nonetheless, it is unlikely that these limitations have affected our main conclusions.

In summary, multiple factors appear to contribute to the higher uterine cancer mortality rate among blacks compared with whites. First, although blacks have a lower incidence of usual types of endometrial carcinoma than do whites, rates for high-grade and advanced-stage tumors of this type are similar, and blacks with these high-grade or advanced-stage tumors fare worse than do whites. Second, blacks have a higher incidence of aggressive types of malignant uterine tumors. Third, blacks have lower survival rates for each type of malignant uterine tumor, including those with favorable prognoses. These data underscore the need for additional studies to determine the etiologies of the less common, more aggressive forms of corpus malignancy, as well as the need for additional investigations to elucidate the causes of racial disparities in incidence and survival.

REFERENCES

1. Grady D, Ernster VL. Endometrial cancer. In: Schottenfeld D, Fraumeni JF, editors. Cancer epidemiology and prevention, 2nd edition. New York: Oxford University Press, 1996.
2. Jemal A, Thomas A, Murray T, Thun M. Cancer statistics, 2002. *CA Cancer J Clin.* 2002;52:23–47.
3. Bach PB, Schrag D, Brawley OW, Galaznik A, Yakren S, Begg CB. Survival of blacks and whites after a cancer diagnosis. *JAMA.* 2002;287:2106–2113.
4. Sherman ME. Theories of endometrial carcinogenesis: a multidisciplinary approach. *Mod Pathol.* 2000;13:295–308.
5. Aziz H, Rotman M, Hussain F, et al. Poor survival of black patients in carcinoma of the endometrium. *Int J Radiat Oncol Biol Phys.* 1993;27:293–301.
6. Bain RP, Greenberg RS, Chung KC. Racial differences in survival of women with endometrial cancer. *Am J Obstet Gynecol.* 1987;157:914–923.
7. Barrett RJ II, Harlan LC, Wesley MN, et al. Endometrial cancer: stage at diagnosis and associated factors in black and white patients. *Am J Obstet Gynecol.* 1995;173:414–423.
8. Hicks ML, Phillips JL, Parham G, et al. The National Cancer Data Base report on endometrial carcinoma in African-American women. *Cancer.* 1998;83:2629–2637.
9. Hill HA, Eley JW, Harlan LC, Greenberg RA, Barrett RJ II, Chen VW. Racial differences in endometrial cancer survival: The Black/White Cancer Survival Study. *Obstet Gynecol.* 1996;88:919–926.
10. Liu JR, Conaway M, Rodriguez GC, Soper JT, Clarke-Pearson DL, Berchuck A. Relationship between race and interval to treatment in endometrial cancer. *Obstet Gynecol.* 1995;86: 486–490.
11. Madison T, Schottenfeld D, Baker V. Cancer of the corpus uteri in white and black women in Michigan, 1985–1994: an analysis of trends in incidence and mortality and their relation to histologic subtype and stage. *Cancer.* 1998;83:1546–1554.
12. Mathews RP, Hutchinson-Colas J, Maiman M, et al. Papillary serous and clear cell type lead to poor prognosis of endometrial carcinoma in black women. *Gynecol Oncol.* 1997;65: 206–212.
13. Ragland KE, Selvin S, Merrill DW. Black-white differences in stage-specific cancer survival: analysis of seven selected sites. *Am J Epidemiol.* 1991;133:672–682.
14. Steinhorn SC, Myers MH, Hankey BF, Pelham VF. Factors associated with survival differences between black women and white women with cancer of the uterine corpus. *Am J Epidemiol.* 1986;124:85–93.
15. Hicks ML, Kim W, Abrams J, Johnson CC, Blount AC, Parham GP. Racial differences in surgically staged patients with endometrial cancer. *J Natl Med Assoc.* 1997;89: 134–140.
16. Plaxe SC, Saltzstein S. Impact of ethnicity on the incidence of high-risk endometrial carcinoma. *Gynecol Oncol.* 1997;65: 8–12.
17. Bokhman JV. Two pathogenetic types of endometrial carcinoma. *Gynecol Oncol.* 1983;15:10–17.
18. Hendrickson M, Ross J, Eifel P, Cox RS, Martinez A, Kempson R. Uterine papillary serous carcinoma: a highly malignant form of endometrial adenocarcinoma. *Am J Surg Pathol.* 1982;6:93–108.
19. Young JL, Ries LG, Pollack ES. Cancer patient survival among ethnic groups in the United States. *J Natl Cancer Inst.* 1984;73:341–352.
20. Coates RJ, Click LA, Harlan LC, Robboy S, Barrett RJ II, Eley JW. Differences between black and white patients with cancer of the uterine corpus in interval from symptom recognition to initial medical consultation (United States). *Cancer Causes Control.* 1996;7:328–336.
21. Harlow BL, Weiss NS, Lofton S. The epidemiology of sarcomas of the uterus. *J Natl Cancer Inst.* 1986;76:399–402.
22. Ries LA, Eisner MP, Kosary CL, et al., editors. SEER cancer statistics review: 1973–1998. Bethesda: National Cancer Institute, 2001.
23. Percy C, Van Holten V, Muir C, editors. International classification of diseases for oncology, 2nd edition. Geneva: World Health Organization, 1990.
24. SEER*STAT [software online] 2001. Available from URL: http://seer.cancer.gov/seerstat
25. Chu KC, Miller BA, Feuer EJ, Hankey BF. A method for partitioning cancer mortality trends by factors associated with diagnosis: an application to female breast cancer. *J Clin Epidemiol.* 1994;47:1451–1461.

26. Sherman ME, Bitterman P, Rosenshein NB, Delgado G, Kurman RJ. Uterine serous carcinoma: a morphologically diverse neoplasm with unifying clinicopathologic features. *Am J Surg Pathol.* 1992;16:600–610.
27. Saraiya M, Lee NC, Blackman D, Smith J, Morrow B, McKenna MA. Self-reported Papanicolaou smears and hysterectomies among women in the United States. *Obstet Gynecol.* 2001;98:269–278.
28. Merrill R. Stat bite: trends in corpus uteri cancer incidence. *J Natl Cancer Inst.* 1996;88:1019.
29. Brett KM, Marsh JVR, Madans JH. Epidemiology of hysterectomy in the United States: demographic and reproductive factors in a nationally representative sample. *J Womens Health.* 1997;6:309–316.
30. Lepine LA, Hillis SD, Marchbanks PA, et al. Hysterectomy surveillance—United States, 1980–1993. *MMWR Morb Mortal Wkly Rep.* 1997;46:1–15.
31. Brett KM, Madans JH. Use of postmenopausal hormone replacement therapy: estimates from a nationally representative cohort study. *Am J Epidemiol.* 1997;145:536–545.
32. Flegal KM, Carroll MD, Kuczmarski RJ, Johnson CL. Overweight and obesity in the United States: prevalence and trends, 1960–1994. *Int J Obes Relat Metab Disord.* 1998;22:39–47.
33. Kamimoto LA, Easton AN, Maurice E, Husten CG, Macera CA. Surveillance for five health risks among older adults—United States, 1993–1997. *MMWR Morb Mortal Wkly Rep.* 1999;48:89–130.
34. Cooper GS, Sandler DP. Age at natural menopause and mortality. *Ann Epidemiol.* 1998;8:229–235.
35. Gold EB, Bromberger J, Crawford S, et al. Factors associated with age at natural menopause in a multiethnic sample of midlife women. *Am J Epidemiol.* 2001;153:865–874.
36. Brinton LA, Barrett RJ, Berman ML, Mortel R, Twiggs LB, Wilbanks GD. Cigarette smoking and the risk of endometrial cancer. *Am J Epidemiol.* 1993;137:281–291.
37. Stanford JL, Brinton LA, Berman ML, et al. Oral contraceptives and endometrial cancer: do other risk factors modify the association? *Int J Cancer.* 1993;54:243–248.
38. Hoyert DL, Freedman MA, Strobino DM, Guyer B. Annual summary of vital statistics: 2000. *Pediatrics.* 2001;108:1241–1255.
39. Mosher WD. Contraceptive practice in the United States, 1982–1988. *Fam Plann Perspect.* 1990;22:198–205.
40. Potischman N, Hoover RN, Brinton LA, et al. Case-control study of endogenous steroid hormones and endometrial cancer. *J Natl Cancer Inst.* 1996;88:1127–1135.
41. Zeleniuch-Jacquotte A, Akhmedkhanov A, Kato I, et al. Postmenopausal endogenous estrogens and risk of endometrial cancer: results of a prospective study. *Br J Cancer.* 2001;84:975–981.
42. Manson JM, Sammel MD, Freeman EW, Grisso JA. Racial differences in sex hormone levels in women approaching the transition to menopause. *Fertil Steril.* 2001;75:297–304.
43. Sherman ME, Sturgeon S, Brinton LA, et al. Analysis of risk factors and hormone levels in patients with uterine serous carcinoma. *Mod Pathol.* 1997;10:963–968.
44. Elit L, Pal T, Goshen R, et al. Familial and hormonal risk factors for papillary serous uterine cancer. *Eur J Gynaecol Oncol.* 2002;23:187–190.
45. Schwartz SM, Weiss NS, Daling JR, et al. Incidence of histologic types of uterine sarcoma in relation to menstrual and reproductive history. *Int J Cancer.* 1991;49:362–367.
46. Zelmanowicz A, Hildesheim A, Sherman ME, et al. Evidence for a common etiology for endometrial carcinomas and malignant mixed mullerian tumors. *Gynecol Oncol.* 1998;69:253–257.